

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently amended) A method for identifying a compound that modulates a heat shock protein (an HSP) - alpha (2) macroglobulin ($\alpha 2M$) receptor-mediated process, comprising:
 - (a) contacting a test compound with: (i) an isolated alpha (2) macroglobulin $\alpha 2M$ receptor, or a ligand binding fragment thereof; and (ii) a purified heat shock protein, or a binding fragment thereof, or a purified HSP-peptide complex; and
 - (b) measuring the level of alpha (2) macroglobulin receptor activity or expression HSP binding activity, HSP uptake activity, or HSP-mediated antigen representation activity,
such that if the level of activity or expression HSP binding activity, HSP uptake activity, or HSP-mediated antigen representation activity measured in (b) differs from the level of alpha (2) macroglobulin receptor activity HSP binding activity, HSP uptake activity, or HSP-mediated antigen representation activity in the absence of the test compound, then a compound that modulates an HSP- $\alpha 2M$ receptor-mediated process is identified.
2. (Previously amended) The method of claim 1, in which the compound identified is an antagonist which interferes with an HSP- $\alpha 2M$ receptor-mediated process.
3. (Currently amended) The method of claim 1, in which the test compound is an antibody specific for the alpha (2) macroglobulin $\alpha 2M$ receptor.
4. (Currently amended) The method of claim 1, in which the test compound is an antibody is specific for alpha (2) macroglobulin.
5. (Currently amended) The method of claim 1, in which the test compound is an antibody is specific for a heat shock protein.

6. (Original) The method of claim 1, in which the test compound is a small molecule.

7. (Original) The method of claim 1, in which the test compound is a peptide.

8. (Currently amended) The method of claim 7, in which the peptide comprises at least 5 consecutive amino acids of the alpha (2) macroglobulin α2M receptor (SEQ ID NO.: 7).

9. (Currently amended) The method of claim 7, in which the peptide comprises at least 5 consecutive amino acids of alpha (2) macroglobulin α2M (SEQ ID NO.: 4).

10. (Original) The method of claim 7, in which the peptide comprises at least 5 consecutive amino acids of a heat shock protein sequence.

11. (Previously amended) The method of claim 1, in which the compound is an agonist which enhances an HSP- α 2M receptor-mediated process.

12. (Currently amended) The method of claim 1 in which the HSP- α 2M receptor-mediated process affects diabetes or other an autoimmune disorder, a disease or disorder involving disruption of antigen presentation or endocytosis, a disease or disorder involving cytokine clearance or inflammation, a proliferative disorder, a viral disorder or other infectious disease, hypercholesterolemia, Alzheimer's disease, diabetes, or osteoporosis.

13. (Currently amended) A method for identifying a compound that modulates an HSP- α 2M receptor-mediated process, comprising:

- (a) contacting a test compound with (i) a cell expressing an alpha (2) macroglobulin α2M receptor or ligand-binding fragment expressing cell and (ii) a purified heat shock protein, or fragment thereof, or a purified HSP-peptide complex; and
- (b) measuring the level of alpha (2) macroglobulin receptor HSP binding activity, HSP uptake activity, or HSP-mediated antigen representation activity in the cell,

such that if the level of alpha (2) macroglobulin receptor HSP binding activity, HSP uptake activity, or HSP-mediated antigen representation activity measured in (b) differs from

the level of alpha (2) macroglobulin receptor HSP binding activity, HSP uptake activity, or HSP-mediated antigen representation activity in the absence of the test compound, then a compound that modulates an HSP- α 2M receptor-mediated process is identified.

14. (Currently amended) The method of claim 1 or 13 wherein the alpha (2) macroglobulin receptor activity HSP binding activity is measured is the ability to bind to a heat shock protein.

15 - 16. (Cancelled)

17. (Currently amended) The method of claim 1 or 13 wherein the alpha (2) macroglobulin receptor activity measured is the ability to bind to a heat shock protein, wherein measuring the level of alpha (2) macroglobulin receptor activity HSP binding activity of step (b) comprises measuring the amount of heat shock protein, or binding fragment thereof, bound to the alpha (2) macroglobulin α 2M receptor, or ligand-binding fragment thereof, such that if the amount of bound heat shock protein measured in (b) differs from the amount of bound heat shock protein measured in the absence of the test compound, then a compound that modulates the binding of an HSP to the α 2M receptor is identified.

18. (Currently amended) The method of claim 1 or 1413, in which the alpha (2) macroglobulin α 2M receptor contacted in step (a) is on a cell surface.

19. (Currently amended) The method of claim 1 or 1413, wherein the alpha (2) macroglobulin α 2M receptor is immobilized to a solid surface.

20. (Original) The method of claim 19 wherein the solid surface is a microtiter dish.

21. (Currently amended) The method of claim 1413, wherein the amount of bound heat shock protein HSP binding activity is measured by contacting the cell with a heat shock protein-specific antibody.

22. (Previously amended) The method of claim 14 wherein the heat shock protein is labeled and the amount of bound heat shock protein is measured by detecting the label.

23. (Original) The method of claim 22 wherein the heat shock protein is labeled with a fluorescent label.

24-63. (Cancelled)

64. (Currently amended) The method of claim 1 or 13, wherein the alpha (2) macroglobulin $\alpha 2M$ receptor is purified.

65-66. (Cancelled)

67. (Currently amended) The method of claim 14, wherein the derivative, analog, $\alpha 2M$ receptor fragment, or domain of the alpha (2) macroglobulin receptor is purified.

68. (Currently amended) A method for identifying a compound that modulates an HSP- $\alpha 2M$ receptor-mediated process, comprising:

- (a) contacting a test compound with (i) an alpha (2) macroglobulin $\alpha 2M$ receptor-expressing cell and (ii) a purified heat shock protein, or fragment thereof, or a purified HSP-peptide complex; and
- (b) measuring the level of alpha (2) macroglobulin $\alpha 2M$ receptor activity by a signal transduction activity assay, heat shock protein uptake assay, chemotaxis assay, or calcium ion concentration assays,

such that if the level of alpha (2) macroglobulin $\alpha 2M$ receptor activity measured in (b) differs from the level of alpha (2) macroglobulin $\alpha 2M$ receptor activity in the absence of the test compound, then a compound that modulates an HSP- $\alpha 2M$ receptor-mediated process is identified.

69. (Currently amended) A method for screening a plurality of molecules for one or more molecules having the ability to modulate, directly or indirectly, the antigen presentation activity of alpha (2) macroglobulin $\alpha 2M$ receptor-expressing cells, comprising:

- (a) contacting said plurality of molecules with said the alpha (2) macroglobulin $\alpha 2M$ receptor-expressing cells and a purified complex of a heat shock protein and the antigenic peptide;
- (b) measuring antigen presentation by said alpha (2) macroglobulin $\alpha 2M$ receptor-expressing cells in the presence of said plurality of molecules; and
- (c) comparing antigen presentation activity by said alpha (2) macroglobulin $\alpha 2M$ receptor-expressing cells in the presence of said plurality of molecules with antigen presentation activity by said alpha (2) macroglobulin $\alpha 2M$ receptor-expressing cells in the absence of said plurality of molecules

wherein a lower or higher degree of antigen presentation indicates that one or more molecule(s) modulates the antigen presentation activity by said alpha (2) macroglobulin $\alpha 2M$ receptor-expressing cells.

70. (Currently amended) A method for screening an antibody specific to a heat shock protein or an alpha (2) macroglobulin $\alpha 2M$ receptor for the ability to modulate, directly or indirectly, the antigen presentation activity alpha (2) macroglobulin $\alpha 2M$ receptor-expressing cells, comprising:

- (a) contacting the antibody with the alpha (2) macroglobulin $\alpha 2M$ receptor-expressing cells and a purified complex of a heat shock protein and the antigenic peptide;
- (b) measuring antigen presentation by the alpha (2) macroglobulin $\alpha 2M$ receptor-expressing cells in the presence of the antibody; and
- (c) comparing antigen presentation activity by said alpha (2) macroglobulin $\alpha 2M$ receptor-expressing cells in the presence of the antibody with antigen presentation activity by the alpha (2) macroglobulin $\alpha 2M$ receptor-expressing cells in the absence of the antibody,

wherein a lower or higher degree of antigen presentation indicates that the antibody modulates the antigen presentation activity by said alpha (2) macroglobulin $\alpha 2M$ receptor-expressing cells.

71. (Currently amended) A method for screening a molecule for the ability to modulate, directly or indirectly, the antigen presentation activity of alpha (2) macroglobulin $\alpha 2M$ receptor-expressing cells, comprising:

- (a) contacting the molecule with purified alpha (2) macroglobulin $\alpha 2M$ receptor-expressing cells and a purified complex of a heat shock protein and an antigenic peptide;
- (b) measuring antigen presentation by the alpha (2) macroglobulin $\alpha 2M$ receptor-expressing cells in the presence of the molecule; and
- (c) comparing antigen presentation activity by the alpha (2) macroglobulin $\alpha 2M$ -expressing cells in the presence of the molecule with antigen presentation activity by the alpha (2) macroglobulin $\alpha 2M$ receptor-expressing cells in the absence of the molecule,

wherein a lower or higher degree of antigen presentation indicates that the molecule modulates the antigen presentation activity by said alpha (2) macroglobulin $\alpha 2M$ receptor-expressing cells.

72. (Currently amended) A method for screening a plurality of molecules for one or more molecules having the ability to modulate, directly or indirectly, the ability of an alpha (2) macroglobulin $\alpha 2M$ receptor-expressing cell to stimulate the activation of activate cytotoxic T cells *in vitro* comprising:

- (a) contacting said plurality of molecules with: (i) cells expressing alpha (2) macroglobulin $\alpha 2M$ receptor; (ii) a purified complex of a heat shock protein and a peptide; and (iii) cytotoxic T cells, under conditions conducive to the activation of cytotoxic T cells;
- (b) comparing the activation *in vitro* of said T cells with the activation *in vitro* of T cells in the absence of said plurality of molecules,

wherein a lower or higher degree of T cell activation indicates that one or more molecules in said plurality of molecules modulates the ability of the alpha (2) macroglobulin $\alpha 2M$ receptor-expressing cells to stimulate the activation of activate cytotoxic T cells against the peptide.

73. (Currently amended) A method for screening an antibody specific to a heat shock protein or an alpha (2) macroglobulin $\alpha 2M$ receptor for the ability to modulate, directly or indirectly, the ability of an alpha (2) macroglobulin $\alpha 2M$ receptor-expressing cell to stimulate the activation of activate cytotoxic T cells *in vitro* comprising:

- (a) contacting the antibody with: (i) cells expressing alpha (2) macroglobulin $\alpha 2M$ receptor; (ii) a purified complex of a heat shock protein and a peptide; and (iii) cytotoxic T cells, under conditions conducive to the activation of cytotoxic T cells;
- (b) comparing the activation *in vitro* of said T cells with the activation *in vitro* of T cells in the absence of said plurality of molecules,

wherein a lower or higher degree of T cell activation indicates that the antibody modulates the ability of the alpha (2) macroglobulin $\alpha 2M$ receptor-expressing cells to stimulate the activation of activate cytotoxic T cells against the peptide.

74. (Currently amended) A method for screening a molecule for the ability to modulate, directly or indirectly, the ability of an alpha (2) macroglobulin α 2M receptor-expressing cell to stimulate the activation of activate cytotoxic T cells in vitro comprising:

- (a) contacting said molecule with: (i) purified cells expressing alpha (2) macroglobulin α 2M receptor; (ii) a purified complex of a heat shock protein and a peptide; and (iii) cytotoxic T cells, under conditions conducive to the activation of cytotoxic T cells;
- (b) comparing the activation in vitro of said T cells with the activation in vitro of T cells in the absence of said plurality of molecules,

wherein a lower or higher degree of activation indicates that one or more molecules in said plurality of molecules modulates the ability of the alpha (2) macroglobulin-expressing cells to ~~stimulate the activation of~~ activate cytotoxic T cells against the peptide.

75. (Previously added) The method of any one of claims 70, 71, or 72, wherein the activity is measured by a cytokine release assay.

76. (Currently amended) The method of any one of claims 13, ~~69, 70, 71, 72, 73,~~ or 74, wherein the alpha (2) macroglobulin α 2M receptor is recombinantly expressed in the cell.

77. (New) The method of claim 1 or 13 wherein HSP uptake activity is measured.

78. (New) The method of claim 1 or 13 wherein HSP-mediated antigen representation activity is measured.

79. (New) The method of any one of claims 69, 70, 71, 72, 73, or 74, wherein the α 2M receptor is recombinantly expressed in the cell.

80. (New) A method for identifying a compound that modulates an HSP- α 2M receptor-mediated process, comprising:

- (a) contacting a test compound with: (i) a ligand-binding fragment of an α 2M receptor; and (ii) a purified heat shock protein, or a binding fragment thereof, or a purified HSP-peptide complex; and

(b) measuring the level of HSP binding activity, HSP uptake activity, or HSP-mediated antigen representation activity,
such that if the level of HSP binding activity, HSP uptake activity, or HSP-mediated antigen representation activity measured in (b) differs from the level of HSP binding activity, HSP uptake activity, or HSP-mediated antigen representation activity in the absence of the test compound, then a compound that modulates an HSP- α 2M receptor-mediated process is identified.

81. (New) The method of claim 80 wherein the ligand-binding fragment of the α 2M receptor is immobilized to a solid surface.

82. (New) The method of claim 80 wherein the ligand-binding fragment of the α 2M receptor contacted in step (a) is on a cell surface.

83. (New) The method of claim 80 wherein the compound identified is an antagonist that interferes with an HSP- α 2M receptor-mediated process.

84. (New) The method of claim 80 wherein the HSP- α 2M receptor-mediated process affects diabetes or other autoimmune disorder, a disease or disorder involving disruption of antigen presentation or endocytosis, a disease or disorder involving cytokine clearance or inflammation, a proliferative disorder, a viral disorder or other infectious disease, hypercholesterolemia, Alzheimer's disease, or osteoporosis.

85. (New) The method of claim 80 wherein the test compound is an antibody specific for the α 2M receptor.

86. (New) The method of claim 80 wherein the test compound is an antibody specific for α 2M.

87. (New) The method of claim 80 wherein the test compound is an antibody specific for a heat shock protein.

88. (New) The method of claim 80 wherein the test compound is a small molecule.

89. (New) The method of claim 80 wherein the test compound is a peptide.

90. (New) The method of claim 89 wherein the peptide comprises at least 5 consecutive amino acids of α 2M (SEQ ID NO.: 4).

91. (New) The method of claim 89 wherein the peptide comprises at least 5 consecutive amino acids of a heat shock protein sequence.

92. (New) The method of claim 89 wherein the peptide comprises at least 5 consecutive amino acids of the α 2M receptor (SEQ ID NO.: 7).

93. (New) A method for identifying a compound that modulates an HSP- α 2M receptor-mediated process comprising:

- (a) contacting a test compound with (i) a cell expressing a ligand-binding fragment of an α 2M receptor and (ii) a purified heat shock protein, or fragment thereof, or a purified HSP-peptide complex; and
- (b) measuring the level of HSP binding activity, HSP uptake activity, or HSP-mediated antigen representation activity in the cell,

such that if the level of HSP binding activity, HSP uptake activity, or HSP-mediated antigen representation activity measured in (b) differs from the level of HSP binding activity, HSP uptake activity, or HSP-mediated antigen representation activity in the absence of the test compound, then a compound that modulates an HSP- α 2M receptor-mediated process is identified.

94. (New) The method of claim 80 or 93 wherein the activity measured is HSP binding activity.

95. (New) The method of claim 94 wherein the heat shock protein is labeled and the amount of bound heat shock protein is measured by detecting the label.

96. (New) The method of claim 94 wherein measuring the level of HSP binding activity of step (b) comprises measuring the amount of heat shock protein, or binding fragment thereof, bound to the ligand-binding fragment of the α 2M receptor, such that if the amount of bound heat shock protein measured in (b) differs from the amount of bound heat shock protein measured in the absence of the test compound, then a compound that modulates the binding of an HSP to the α 2M receptor is identified.

97. (New) The method of claim 93 wherein the ligand-binding fragment of the $\alpha 2M$ receptor contacted in step (a) is on the surface of the cell.

98. (New) The method of claim 93 wherein the HSP binding activity is measured by contacting the cell with a heat shock protein-specific antibody.

99. (New) The method of claim 93 wherein the cell expressing the ligand-binding fragment of the $\alpha 2M$ receptor is immobilized to a solid surface.

100. (New) The method of claim 99 wherein the solid surface is a microtiter dish.

101. (New) The method of claim 100 wherein the heat shock protein, or fragment thereof, or the purified HSP-peptide complex, is labeled with a fluorescent label.

102. (New) The method of claim 93 wherein the ligand-binding fragment of the $\alpha 2M$ receptor is recombinantly expressed in the cell.

103. (New) The method of claim 93 wherein the activity measured in step (b) is measured by a signal transduction activity assay, a heat shock protein uptake assay, a chemotaxis assay, or a calcium ion concentration assay.

104. (New) The method of claim 80 or 93 wherein the ligand-binding fragment of the $\alpha 2M$ receptor is purified.

105. (New) The method of claim 80 or 93 wherein HSP uptake activity is measured.

106. (New) The method of claim 80 or 93 wherein HSP-mediated antigen representation activity is measured.

107. (New) The method of claim 80 or 93 wherein the ligand-binding fragment of the $\alpha 2M$ receptor comprises at least one complement repeat.

108. (New) The method of claim 107 wherein at least one complement repeat is selected from the group consisting of CR3 to CR10.

109. (New) The method of claim 80 or 93 wherein the ligand-binding fragment of the $\alpha 2M$ receptor comprises a cluster of complement repeats.

110. (New) The method of claim 80 or 93 wherein the cluster of complement repeats comprises the CI-CII complement repeat cluster of the α 2M receptor.

111. (New) The method of claim 80 or 93 wherein the ligand-binding fragment of the α 2M receptor comprises the p80 fragment of the α 2M receptor.

112. (New) The method of claim 80 or 93 wherein the ligand-binding fragment of the α 2M receptor is a peptide consisting of amino acids selected from the group consisting of the following amino acids of the human α 2M receptor: 25-68 (SEQ ID NO:20), 25-110 (SEQ ID NO:21), 68-110 (SEQ ID NO:22), 853-894 (SEQ ID NO:23), 853-934 (SEQ ID NO:24), 853-974 (SEQ ID NO:25), 853-1013 (SEQ ID NO:26), 853-1060 (SEQ ID NO:27), 853-1102 (SEQ ID NO:28), 853-1183 (SEQ ID NO:29), 895-934 (SEQ ID NO:30), 895-974 (SEQ ID NO:31), 895-1013 (SEQ ID NO:32), 895-1060 (SEQ ID NO:33), 895-1102 (SEQ ID NO:34), 895-1183 (SEQ ID NO:35), 935-974 (SEQ ID NO:36), 935-1013 (SEQ ID NO:37), 935-1060 (SEQ ID NO:38), 935-1102 (SEQ ID NO:39), 935-1183 (SEQ ID NO:40), 975-1013 (SEQ ID NO:41), 975-1060 (SEQ ID NO:42), 975-1143 (SEQ ID NO:43), 975-1183 (SEQ ID NO:44), 1014-1060 (SEQ ID NO:45), 1014-1102 (SEQ ID NO:46), 1014-1183 (SEQ ID NO:47), 1061-1102 (SEQ ID NO:48), 1061-1143 (SEQ ID NO:49), 1061-1183 (SEQ ID NO:50), 1103-1143 (SEQ ID NO:51), 1103-1183 (SEQ ID NO:52), and 1144-1183 (SEQ ID NO:53).